REMARKS

Claims 1, 5, 6, 8-18, 20, 21, 23, 25, and 27 were pending in the subject application. Claims 1, 5, 11, 12, 14, 16-18, 20, 21, 23, 25, and 27 were withdrawn from consideration by the Examiner as being drawn to nonelected inventions.

Applicants have hereinabove amended claims 1, 6, 11, 15, and 17 and have added claims 28-29.

Support for the amendment to claims 1, 6, 11, 15 and 17 to require 80% identity to the recited sequence is to be found, *inter alia,* in the description as filed at page 8, line 33. Support for the amendment to claim 6 to recite the features of claim 1 is to be found in claim 1 as filed. Support for the amendment to claim 6 to require that the polynucleotide encodes a peptide having antifungal and/or antibacterial activity is to be found, *inter alia,* in the description as filed at page 6, lines 1 and 2. Support for newly added claim 28 is to be found, *inter alia,* in the description as filed at page 2, lines 11-33. Support for newly added claim 29 is to be found, *inter alia,* in the description as filed at page 2, lines 11-33, page 5, lines 17-37, and page 6, lines 1-9.

We have also amended claims 1, 11 and 15 to delete reference to the term "fragment" in the final clause of the claim. We propose that the recitation in clause ix) that the claimed peptide includes biologically active fragments encompasses the deleted subject matter. Please enter this amendment if it will not raise an issue of file wrapper estoppel. Alternatively, please amend the term "fragment" to read "the biologically active fragment".

Election/Restriction

The Examiner has maintained his allegation that claims defining peptides and claims defining nucleic acids constitute different

inventions and that each of the exemplified sequences constitutes a separate invention. We would prefer to argue further against this requirement for restriction at this stage.

Turning first to the Examiner's allegation that claims 1, 5, 12 and 27 (defining peptides) and claims 6, 8-10 and 13 (defining nucleic acids) constitute separate inventions, this application is a '371 US national phase application and, as a consequence, unity of invention **must** be assessed under PCT Rule 13. Annex B of Appendix AI entitled "Administrative instructions under the PCT" of the Manual of Patent Examining Procedure provides detailed guidelines of the determination of unity of invention for "371" US national phase application. Annex B provides a number of examples where the determination of unity of invention varies between Rule 13 of the PCT Regulations and US practice. Section (1) directs the Examiner to the "PCT International Search and Preliminary Examination Guidelines" which provides further examples of how the principles of Rule 13 **should be** applied. Chapter 10 of the PCT International Search and Preliminary Examination Guidelines relates to unity of invention. Paragraphs 10.20 to 10.59 provide yet further detailed examples of the determination of unity of invention under PCT Rule 13. As discussed in Section 10.59, where there is no prior art disclosing the claimed polynucleotide or peptide, the claimed polynucleotide and peptide share a corresponding technical feature. "Consequently, the claims have unity of invention (*a priori*)".

As discussed previously, the prior art relied on by the Examiner to support his allegation of lack of unity of invention (Schuhman *et al., Arch. Insect. Biochem. Physiol., 53*: 125-133, 2003) discloses a peptide having 33.3% sequence identity to SEQ ID NO: 4 over a very small 12 amino acid stretch (rather than the entire sequence) and about the same level of identity to other sequences defined in claim 1. In contrast, the claims as amended require at least 80% identity. Accordingly, there is no prior art disclosing the

sequences recited in claims 1, 5, 6, 8-10, 12, 13 and 27 and in applying the PCT Guidelines discussed above, claims defining peptides and polynucleotides must have unity of invention (*a priori*). The same principle applies to claims defining host cells, non-human animals, vectors and processes making use of the claimed peptides, polypeptides, plants and for making the claimed peptides.

As for the Examiner's contention that each sequence constitutes a separate invention, we submit that each of the claimed peptides is an alternative in a class of peptides sharing a common property and a common structure. For example, as discussed at page 42 of the instant application, the peptides of the present invention share a long linear alpha-helical tertiary structure, part of which is amphipathic. Furthermore, the claimed peptides are similar at the amino acid level as evidenced by the specification including a consensus sequence for the peptides of the invention (SEQ ID NO:62). The claimed polynucleotides also share a common property because they encode peptides having the shared common property and structure. Moreover, as previously discussed, this structure is entirely different to that of the defensin peptide/nucleic acid disclosed in the prior art relied on by the Examiner to support his allegation of lack of unity of invention. Accordingly, the sequences defined in the claims constitute a proper Markush group as required in Annex B paragraph f of Appendix AI entitled "Administrative instructions under the PCT" of the Manual of Patent Examining Procedure. As discussed in that section, if the alternatives claimed share a common property or a common structure, they shall be considered "of a similar nature" and "the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2 shall be considered to be met".

Finally, the Examiner's assertion that the technical feature linking each of the sequences is that they are antimicrobial peptides from

Galleria mellonella overlooks the feature that these peptides are related peptides from *G. mellonella*, which belong to a separate class of peptides to the **defensin** peptide of the prior art and is distinguished at the primary structural level (i.e., sequence) and at the secondary and tertiary structural levels.

Based on the foregoing, we request rejoinder of claims 1-21 and 27.

Priority

The Examiner has acknowledged receipt of the papers submitted under 35 U.S.C 119(a)-(d). The Examiner indicates that the papers have been placed of record in the file.

Information Disclosure Statement

Applicant acknowledges that the Examiner has considered and made of records the references submitted with the Information Disclosure Statements filed on August 24, 2006, June 1, 2007, and July 21, 2008 as indicated on the PTO Forms 1449 included with the October 10, 2008 Office Action.

Specification

In the October 10, 2008 Office Action, the Examiner indicated that the proprietary nature of trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

In response, applicants have hereinabove amended the specification to identify trademarks in uppercase and to provide a generic description of the product identified by the trademark where necessary. Applicants maintain that the amendments to the specification add no new matter.

Claim Objection

Claim 6 is objected to as being dependent on a withdrawn claim (claim 1). We have now amended claim 6 to delete reference to claim 1 and to incorporate all of the structural limitations of claim 1, thereby overcoming this objection.

Claim Rejections - 35 U.S.C §112

The Examiner has alleged that the specification provides insufficient written description of the subject matter of claim 15. The Examiner's objection appears to be based on his opinion that the specification provides insufficient guidance as to specific variants and fragments of the claimed sequences that will have the antibacterial and/or antifungal activity required by the claims, and provides no description of polynucleotides that hybridize to those claimed and encodes a peptide having the requisite activity. The Examiner also alleges that the specification only provides a sufficient structure of the chemical structure of the peptides set forth in SEQ ID NOs: 1, 4 and 9.

We assume that this rejection will now apply to all claims of the application given our amendment to introduce the requirement that the claims polynucleotides encode a peptide having antibacterial and/or antifungal activity.

We have now deleted clauses in the claims directed to hybridization under high stringency conditions, rendering this aspect of the rejection moot.

We traverse the Examiner's objection. Firstly, please direct the Examiner's attention to Example 11a of the USPTO's Written Description Training Materials (March 1, 2008), which clearly states

that a specification provides sufficient written description of a nucleic acid encoding a protein having at least 85% identity to protein X (which is the only sequence disclosed in a specification) and having activity Y, if the specification identifies regions required for the biological activity of protein X and *postulates* that conservative substitutions in those regions might maintain biological activity.

We submit that the present specification provides more detailed information than is required in the example above and, as a consequence, satisfies the written description requirement. For example, the specification provides the sequence of the elected peptide (SEQ ID NO: 4) and its precursor form (SEQ ID NO: 1) and polynucleotides encoding SEQ ID NO: 1 and SEQ ID NO: 4 and an allelic variant of said polynucleotide. Furthermore, the specification provides the sequence of *three (3)* additional *G. mellonella* related peptides and encoding polynucleotides, which share between 42% and 89% identity at the amino acid level and 57% and 90% identity at the nucleotide level. Accordingly, the specification describes a class of peptides having a lower degree of sequence identify than is actually required by the claims. The skilled artisan will be readily able to predict additional sequences using current computer technology (as taught in the USPTO's Training Manual).

Furthermore, the specification discusses the various structural elements of the peptides that are important for biological activity. For example, at page 42 the specification describes the moricin peptides as comprising a helical structure comprising hydrophobic residues at the C terminal end of the helix and an amphipathic region comprising basic amino acids that the N-terminal end of the helix and a C-terminus comprising charged amino acids.

The specification also provides a consensus sequence of the claimed

G. mellonella moricin peptides based on the variety of distinct peptides isolated by the inventors (SEQ ID NO: 62), which clearly indicates sites at which substitutions can be made, and which substitution can be made. As discussed in the Training Materials, whilst not all of the recited substitutions may result in a peptide having the requisite activity, based on the teachings in the specification those of ordinary skill in the art would expect that many of these substitutions would result in a protein having the required activity.

Accordingly, following the Training Materials set out by the USPTO, the specification provides the sequence of several peptides structurally related at the tertiary level (i.e., more than the one actually required), identifies structural regions that are important for biological activity and further identifies specific sites at which amino acid residues can be substituted while retaining biological activity. Accordingly, the specification satisfies the USPTO's guidelines as to the requirements of written description, and we request withdrawal of this rejection.

Enablement

The Examiner also alleges that claims 6, 8-10, 13 and 15 are not enabled. Our reading of the Office Action indicates that the Examiner's rejection is based on the following reasoning:

(i) most claims do not require that the claimed peptides have antibacterial and/or antifungal activity;

(ii) the claims encompass any polynucleotide or polypeptide that comprises two residues of the recited sequences;

(iii) the specification only discloses SEQ ID NO: 4 and its encoding polynucleotides and does not disclose sequences having 66% identity thereto having antibacterial and/or antifungal activity and that it is not possible to predict where suitable substitutions can be made (e.g., using computational

processes);

(iv) the specification does not disclose any sequences that hybridize under highly stringent conditions to the recited sequence and encode a peptide having antibacterial and/or antifungal activity; and

(v) the production of transgenic animals is highly unpredictable.

We have now cancelled clauses in the claims requiring hybridization under highly stringent conditions, rendering this aspect of the rejection moot.

We have also amended all claims to require that the claimed peptides (including biologically active fragments thereof) having antibacterial and/or antifungal activity.

Notwithstanding that we believe that it was clear that the claims as filed only encompassed biologically active fragments of the recited peptides by virtue of clause ix), we have now entered an amendment to clarify this fact. The term biologically active is defined in the specification as maintaining a biological activity of the full length peptide, in this case antibacterial and/or antifungal activity as required by the claims. Accordingly, the claims do not encompass any fragment of the recited sequences including fragments of only two amino acids, since those fragments would not have the requisite biological activity.

In contrast to the Examiner's allegation that the specification only enables SEQ ID NO: 4 and its encoding polynucleotides and not sequences having a degree of % identity thereto, we submit that the specification clearly discloses a variety of peptides related at the secondary and/or tertiary level which share between 42% and 89% identity at the amino acid level. The specification also demonstrates that these peptides have antibacterial and/or antifungal activity. Accordingly, the specification enables

production of peptides having far less identity than the 80% recited in the claims as amended.

Furthermore, as discussed in detail above, the specification clearly teaches a consensus sequence that shows which amino acids may be substituted, or which amino acids may be omitted (e.g., in a fragment), see SEQ ID NO: 62. This consensus sequence was not based on computational predictions as the Examiner appears to believe, but on the sequence of peptides actually shown to have the requisite activity. Furthermore, the specification teaches the desired secondary/tertiary structure of a peptide of the invention and the residues involved in attaining that structure, e.g., at page 42. Based on the teaching in SEQ ID NO: 62 and/or the teaching at page 42, the skilled artisan would readily be able to determine peptides having antibacterial and/or antifungal activity. The skilled artisan would also be able to assess the activity of those peptides using methods exemplified in the instant application, e.g., at page 31, lines 21 to 32.

As for the Examiner's allegation that the production of transgenic non-human animals is unpredictable, we respectfully traverse. The citations relied upon by the Examiner in attempting to establish that production of transgenic animals is unpredictable merely establishes that the genetic background of the transgenic organism (e.g., an inbred mouse) effects the phenotypic effect of the transgene. One of these references (Brampton *et al., Brain Res. 841*: 123-134, 1999) does not even actually produce transgenic animals, instead performing experiments on unmodified inbred mice.

Techniques for producing transgenic animals have been in use for over 20 years (e.g., pronuclear microinjection-based methods), and are now standard practice. We submit Rülicke and Hübscher *Exp. Physiol 85 (6):* 589 (2000), which clearly teaches that whilst the frequency of transgenic founders produced using art recognized

methods may vary between species, it "is efficient enough to render this technique applicable to a wide range of mammals" (see Abstract).

We request that the Examiner withdraw his rejection in view of the foregoing comments.

Clarity

The Examiner has also rejected claims 6, 8-10 and 15 as being indefinite as a result of the term "high stringency conditions".

This term has been deleted from the claims thereby rendering this objection moot.

Novelty

The Examiner alleges that claims 6, 8-10, 13 and 15 lack novelty over the disclosure in WO 02/086072 (Altier et al) of a polynucleotide 3 consecutive nucleotides in common with SEQ ID NO: 9 and three consecutive amino acids in common with SEQ ID NO: 4.

As discussed above, we have amended the claims to clarify that the fragments defined are biologically active (i.e., the fragment itself must have antibacterial and/or antifungal activity). The 3 amino acid region of the peptide disclosed in Altier et al that is homologous to a region of a peptide disclosed in the instant application could not have the antibacterial and/or antifungal activity required by the claims as amended (i.e., it could not form the secondary/tertiary structure required to exert such biological activity). Nor does Altier disclose a peptide or polynucleotide having 80% identity to a sequence recited in the present claims. Accordingly Altier does not disclose a peptide or a *biologically active* fragment thereof or polynucleotide encoding same as required

by the claims of the instant application, and all claims are novel over this disclosure.

Supplemental Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following document listed below which is also listed on the Form PTO-1449 (Substitute) attached hereto as **(Exhibit A)**.

This Supplemental Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97 (c)(2) before the mailing of a final office action. Pursuant to C.F.R. §1.17(p) the fee for filing this Supplemental Information Disclosure Statement is $180.00.

A copy of item 1 is attached hereto as **Exhibit 1.**

Applicants request that the document listed below and on the Form PTO-1449 (Substitute) be considered and made of record in the above-identified application.

1. Rülicke, T. and Hübscher, U., "Germ line transformation of mammals by pronuclear microinjection," *Experimental Physiology* (2000) 85(6), 589-601 (**Exhibit 1**).

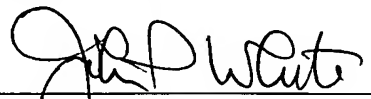
Conclusion

Applicants respectfully submit that all grounds of rejection set forth in the October 10, 2008 Office Action have been overcome. Applicants therefore respectfully request that the Examiner reconsider and withdraw these grounds of rejection, and earnestly solicit allowance of all claims pending in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

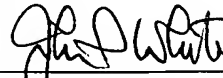
No fee, other than the enclosed $890.00 including a $490.00 fee for a 2-month extension of time, and a $180.00 fee for filing a Supplemental Information Disclosure Statement before the issuance of a Final Office Action, and a $220.00 additional fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham LLP
30 Rockefeller Plaza
New York, New York 10112
Tel. No. (212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450



3/10/09

John P. White Date
Reg. No. 28,678

EXHIBIT A

EXHIBIT 1